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| 10/594,740 | 12/01/2006 | Bernard Freiss | 3493-0179PUS1 | 5296 |

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| EXAMINER | |
|---|---|
| LAU, JONATHAN S | |

| ART UNIT | PAPER NUMBER |
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| 1623 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,740 | FREISS ET AL. | |
| | Examiner | Art Unit | |
| | Jonathan S. Lau | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 Jun 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-21 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 Jun 2009 has been entered.

This Office Action is responsive to Applicant's Amendment and Remarks, filed 22 Jun 2009, in which claims 11 and 20 are amended to clarify the scope and breadth of the claims.

This application is the national stage entry of PCT/FR05/00739, filed 29 Mar 2005; and claims benefit of foreign priority document FRANCE 0403450, filed 01 Apr 2004, and foreign priority document FRANCE 0411201, filed 21 Oct 2004; currently English language translations of these foreign priority document have not been filed.

Claims 11-21 and 26 are pending.

The following are modified grounds of rejection.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 11-21 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) as evidenced by Van Hees et al. 1999 (Pharmaceutical Research, 1999, 16, p1864-1870, provided by Applicant on IDS filed 29 Sep 2006) and in view of Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record).

Van Hees et al. 2002 discloses preparing complexes of piroxicam and β-cyclodextrin using super-critical $CO_2$ ($SCCO_2$) (page 271, left column, lines 9-10), the inclusion compound of an active substance whose aqueous solubility is poor and a host

molecule in a dense pressurized fluid. Van Hees et al. 2002 discloses the process using the technique described in Van Hees et al. 1999 (Van Hees et al. 2002, page 271, right column, lines 6-8), and Van Hees et al. 1999 discloses the process of bringing the active substance, piroxicam, in contact with the host molecule, β-cyclodextrin, pressurized and exposed to $SCCO_2$ in the static mode and recovering the molecular complex formed (Van Hees et al. 1999, page 1865, left column, paragraph Preparation of Inclusion Complexes). Van Hees et al. 2002 discloses the addition of agents for interaction with the complex such as L-lysine, an amino acid that is a base, and the non-preferred aqueous ammonium hydroxide solution (page 273, right column, lines 15-20), as well as the use of citric acid, a carboxylic acid (page 274, right column, line 2). Van Hees et al. 2002 discloses the process performed at pressures between 15-30 and 45 MPa and a temperatures of 125-137 and 150 °C (page 271, right column, paragraph Preparation of complexes using $SCCO_2$). Van Hees et al. 1999 discloses the extraction vessel in the apparatus for performing the molecular diffusion of piroxicam and β-cyclodextrin does not include a stirring mechanism (Van Hees et al. 1999, page 1865, left column, Fig. 1. Schematic diagram of the apparatus).

Van Hees et al. 2002 does not specifically disclose the process wherein the molecular diffusion is performed in the presence of one or more diffusion agents (instant claim 11), wherein said diffusion agent is chosen from the group consisting of alcohols, ketones, ethers, esters and water, with or without surfactant, and their mixtures (instant claim 19), or wherein the diffusion agent is added continuously or portionwise in an amount of between 1 and 50% by weight (instant claim 21). Van Hees et al. 2002 does

not specifically disclose the process including the step of recovering the active substance/host molecule molecular complex thus formed prior to adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex and recovering the soluble inclusion compound thus formed (instant claim 11).

Junco et al. teaches the complexation of a pharmaceutically active substance with β-cyclodextrin using super-critical $CO_2$ (page 69, abstract). Junco et al. teaches the addition of a small amount of co-solvent to a supercritical fluid can have dramatic effects on its solvent power (page 70, left column, lines 4-6). Junco et al. specifically teaches the use of co-solvents ethyl acetate, acetone, methanol, ethanol, 1-propanol and 2-propanol (page 70, left column, lines 6-11). Junco et al. teaches the use of ethanol added continuously in the amount of 4% by weight (page 70, right column, line 17).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process of preparing complexes of piroxicam and β-cyclodextrin using super-critical $CO_2$ disclosed by Van Hees et al. 2002 with the addition of a small amount of co-solvent, or diffusion agent, taught by Junco et al. Both Van Hees et al. 2002 and Junco et al. are drawn to the process of preparing complexes of an active agent and β-cyclodextrin using super-critical $CO_2$. One of ordinary skill in the art would have been motivated to combine the process disclosed by Van Hees et al. 2002 with teaching of Junco et al. because Junco et al. teaches the solubility

enhancement with these co-solvents is considerable (Junco et al. page 70, left column, lines 10-11).

With regard to the process including the step c. of recovering the active substance/host molecule molecular complex thus formed prior to step d. adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex and step e. recovering the soluble inclusion compound thus formed (instant claim 11), MPEP 2144.04 IV. C. states "selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results." The instant specification, examples 2-5 spanning pages 27-28 make comparison with the process using only aqueous ammonia. Van Hees et al. 2002 teaches the process wherein the step (d) carried out under pressure in the presence of the dense pressurized fluid. The invention as recited in the claims is interpreted to encompass the process wherein the step (d) is carried out under pressure in the presence of the dense pressurized fluid. Therefore the results of the experiments disclosed in the instant specification are not commensurate with the scope of the claims because the invention encompassed by the scope of the claims includes the process wherein the step (d) is carried out under pressure in the presence of the dense pressurized fluid.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 22 Jun 2009, have been fully considered and not found to be persuasive.

Applicant notes that the commonly accepted meaning of "recovering" in chemistry is to separate the product of a reaction from the reactants. The ordinary definition of recovering (definition of recover, Merriam-Webster OnLine Dictionary, cited in PTO-892) encompasses "1: to get back: regain", "5 : to find or identify again <*recover* a comet>" and "6 a: to obtain from an ore, a waster product, or a by-product". Therefore the ordinary meaning of recovering encompasses both obtaining, as by separation or isolation, of a product and getting back or identifying a product without necessarily separating or isolating the product. While the term is interpreted within context of the chemical arts, the definition within the chemical arts is not limited to separation or isolation as defined within the chemical arts, therefore the ordinary definition is encompassed by the term.

Applicant remarks that there is a depressurization between steps (b) and (d) in the instant invention and that step (d) is not carried out under pressure or in the presence of the dense pressurized fluid. However, these limitations are not found within the claims. Van Hees et al. 2002 as evidenced by Van Hees et al. 1999 and in view of Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) renders obvious as above the process wherein the step (d) carried out under pressure in the presence of the dense pressurized fluid. The invention as recited in the claims is interpreted to encompass the process wherein the step (d) is carried out under pressure in the presence of the dense pressurized fluid.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended Claims 11-22 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 13 of copending Application No. 10/554,058 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006). Both instant claims 11-22 and claims 1-10 and 13 of copending Application No. 10/554,058 are drawn to the process of preparation of a soluble inclusion compound by bringing the active substance that is a small organic molecule into contact with a host molecule that is cyclodextrin in static mode and carrying out molecular diffusion in a dense pressurized fluid such as super-critical $CO_2$.

Claims 1-10 and 13 of copending Application No. 10/554,058 do not specifically disclose adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

Van Hees et al. 2002 teaches as above. Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance such as L-lysine, or an agent for interaction with the complex, is added (page 274, left column, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex as taught by Van Hees et al. 2002. One of ordinary skill in the art would be motivated to combine the process disclosed in Claims 1-10 and 13 of copending Application No. 10/554,058 with the teachings of Van Hees et al. 2002 because Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance, or agent for interaction with the complex, is added.

This is a provisional obviousness-type double patenting rejection.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 22 Jun 2009, have been fully considered and not found to be persuasive.

Applicant remarks that the instant invention constitutes two reaction steps, as there is a depressurization between steps (b) and (d) in the instant invention and that step (d) is not carried out under pressure or in the presence of the dense pressurized

fluid. However, these limitations are not found within the claims. Claims 1-10 and 13 of copending Application No. 10/554,058 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) renders obvious as above the process wherein the step (d) carried out under pressure in the presence of the dense pressurized fluid. The invention as recited in the claims is interpreted to encompass the process wherein the step (d) is carried out under pressure in the presence of the dense pressurized fluid.

As this provisional obviousness-type double patenting rejection is not the only remaining grounds of rejection, it is proper to maintain this modified provisional rejection.

Amended Claims 11-21 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,390,411, now issued from copending Application No. 10/492,346, in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006). Instant claims 11-22 and claims 1-8 of U.S. Patent No. 7,390,411 are drawn to the process of preparation of a soluble inclusion compound by bringing the active substance that is a small organic molecule into contact with a host molecule, or porous support, that is cyclodextrin, in static mode and carrying out molecular diffusion in a dense pressurized fluid such as super-critical $CO_2$.

Claims 1-8 of U.S. Patent No. 7,390,411 do not specifically disclose adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex.

Van Hees et al. 2002 teaches as above. Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance such as L-lysine, or an agent for interaction with the complex, is added (page 274, left column, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the process disclosed in claims 1-8 of U.S. Patent No. 7,390,411 with adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex as taught by Van Hees et al. 2002. One of ordinary skill in the art would be motivated to combine the process disclosed in claims 1-8 of U.S. Patent No. 7,390,411 with the teachings of Van Hees et al. 2002 because Van Hees et al. 2002 teaches the inclusion yield is significantly higher when a ternary alkaline substance, or agent for interaction with the complex, is added.

**Response to Applicant's Remarks:**

Applicant's Remarks, filed 22 Jun 2009, are relevant to the above rejection of amended claims 11-21 and 26 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,390,411, now issued from copending Application No. 10/492,346, in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006).

Applicant remarks that the instant invention constitutes two reaction steps, as there is a depressurization between steps (b) and (d) in the instant invention and that step (d) is not carried out under pressure or in the presence of the dense pressurized fluid. However, these limitations are not found within the claims. Claims 1-8 of U.S. Patent No. 7,390,411 in view of Van Hees et al. 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006) renders obvious as above the process wherein the step (d) carried out under pressure in the presence of the dense pressurized fluid. The invention as recited in the claims is interpreted to encompass the process wherein the step (d) is carried out under pressure in the presence of the dense pressurized fluid.

The following are new grounds of rejection.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 11-21 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the process comprising step d. wherein mixing the active agent/host molecule molecular complex and the agent for interaction with the complex is a solution, does not reasonably provide enablement for the process comprising step d. wherein mixing the active agent/host molecule molecular complex and the agent for interaction with the complex are both solid

materials. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A process for the preparation of a soluble inclusion compound comprising one or more active substances included in one or more host molecules, the active substance or substances not being very soluble in an aqueous medium comprising step d. carrying out a step which consists in adding to an mixing with the active substance/host molecule molecular complex an agent for interaction with the complex. Applicant's Remarks, filed 22 Jun 2009, state at page 6, paragraph 1 that the step (d) is not carried out under pressure or in the presence of the dense pressurized fluid.

The state of the prior art: It is well known in the chemical arts that molecular interaction requires proximity between particles. It is well known that in the chemical arts that diffusion in solution, such as in aqueous or supercritical $CO_2$ solvent, readily

brings particles into proximity. It is well known that in the chemical arts that a mixture of solid particles provides minimal interaction only between surface layers of the bulk particles.

The prior art Van Hees et al. 2002 teaches the an agent for interaction with the complex interacting with the active substance/host molecule molecular complex in the reaction medium of the dense pressurized fluid supercritical $CO_2$ as recited above.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The sheer number of possible host-guest molecular complexes and agents for interaction with the complex means that one skilled in the art cannot predict the usefulness for all possible solid-solid interactions. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible chemical structure could potentially be used as agent for interaction with the complex.

The amount of direction or guidance presented: The specification speaks generally about the properties of the agent for interaction with the complex, such as improving the property of dissolution in an aqueous medium. Examples of a surfactant such as sodium lauryl sulfate, L-arginine, citric acid and aqueous ammonia are given at pages 9-10. However, guidance is not given for solution phase agents for interaction with the complex other than aqueous ammonia.

The presence or absence of working examples: The only working examples provided are for the solution aqueous ammonia.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as solid-solid interactions between any host-guest molecular complex and any agent for interaction with the complex. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible host-guest molecular complexes and agents for interaction with the complex beyond those known in the art (such as when the interaction is done in presence of a solvent such as water or supercritical $CO_2$), one skilled in the art would undertake a novel and extensive research program into solid-solid interactions. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of possible host-guest molecular complexes and agents for interaction with the complex, it would constitute an undue and unpredictable experimental burden.

> *Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for all possible processes comprising step d. wherein mixing the active agent/host molecule molecular complex and the agent for interaction with the complex is not a solution in view of Applicant's Remarks, filed 22 Jun 2009, in which it is stated at page 6, paragraph 1 that the step (d) is not carried out under pressure or in the presence of the dense pressurized fluid.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-21 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11, reciting the term "soluble inclusion compound" at line 1, is found to be indefinite upon further reconsideration of the language of the invention as claimed. Claims 12-21 and 26 depend from claim 11 and incorporate all limitations therein. The claims are indefinite because it is unclear what solvent said inclusion compound is soluble in. Claim 11 recites the active substance is not very soluble in an aqueous medium, but does not require the solubility of said "soluble inclusion compound" to be an aqueous solubility. One of skill in the art would not be readily apprised of the metes and bounds of the claim because it is unclear what inclusion compound is made by the instantly claimed process because it is unclear which solvent said inclusion compound is soluble in.

Claim 17, reciting "anilide derivatives" at line 2 and "epipodophyllotoxin derivatives" at lines 2-3, is found to be indefinite upon further reconsideration of the invention as claimed in view of Applicant's remarks regarding the closest prior art compared to the specific embodiments disclosed in the specification and the scope of the invention as claimed. Post art Moribe et al. (J. Incl. Phenom Macrocycl. Chem. 2007, 57, p289-295, cited in PTO-892) discloses that drug complexation depended both

on supercritical $CO_2$ (SC-$CO_2$) treatment time and on drug solubility in $CO_2$ (page 289, abstract). Moribe et al. discloses that the intrinsic poor solubility of an active pharmaceutical ingredient often makes it difficult to prepare the desired product (page 289, right column, paragraph 1). Moribe et al. discloses the operating conditions, such as pressure, temperature and processing time also contribute to the complex formation rate (page 294, left column, paragraph 4). Moribe et al. discloses the dissolution of both the pharmaceutical ingredient and the host molecule, TM-β-CD, are rate-determining steps for the formation of the inclusion complex and that the formation of a complex depends on the solubility of the pharmaceutical ingredient (page 294, left column, section Conclusions). Post art Galia et al. (J. Phys. Chem. B 2007, 111, p2573-2578, cited in PTO-892) discloses that use of supercritical $CO_2$ ($scCO_2$) as a reaction medium is often restricted by the poor solubility of substrates in this solvent (page 2573, left column, paragraph 1) and discloses the field of host-guest interactions of β-CD in $scCO_2$ remains a largely unexplored field and studies to gain better comprehension of host-solvent and guest-solvent interactions are necessary (page 2573, right column, paragraph 2). Galia et al. discloses considerations of the steric fit between the host and guest are valid in the case of complexation in $scCO_2$ (page 2577, right column, paragraph 3). The state of the art teaches the steric fit between the host and guest molecule and the solubility of the pharmaceutical ingredient in the dense pressurized fluids of the reaction medium are considerations of the formation of the complex, and it is unclear how what derivatives are encompassed by the term “anilide derivatives” or “epipodophyllotoxin derivatives” and how any changes would affect the steric fit

between the host and guest molecule and the solubility of the pharmaceutical ingredient in the dense pressurized fluids of the reaction medium. Therefore one of skill in the art would not be readily apprised of the metes and bounds of the invention as claimed with regard to the term "anilide derivatives" or "epipodophyllotoxin derivatives" in view of the requirements of host and guest molecules and solvent interactions encompassed by the scope of the invention as claimed.

***Conclusion***

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Shaojia Anna Jiang/
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